BrdU labeled cells 18.72±7.25, 12.80±4.58 and 0.74±0.56 at 1, 3 and 23 weeks respectively which correspond to the proliferation rate, was negligible after 23 weeks.
Conclusions: The cellular growth over the filtering struts of the Diverter converges and reaches steady state within 6 months. Permanent arterial filtration by percutaneous implantation of the fine wire based Diverter is feasible and free of risk of cellular overgrowth and lumen obliteration. Our preliminary findings give hope for a new promising strategy for preventing embolic stroke. The approach would be particularly useful in elderly patients with chronic atrial fibrillation and contra-indications to anti-coagulation.

POSTER SESSION

1181 Non-Low-Density Lipoprotein Cholesterol Effects of Statin Therapy

Tuesday, April 01, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: 1:00 p.m.-2:00 p.m.

1181-120 Statins Promote Systemic Antioxidant Effects Through Specific Inflammatory Pathways

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Background: Formation of nitric oxide-derived oxidants and oxidative cross-linking of proteins both serve as potential mechanisms linking inflammation to development of atherosclerosis. Nitrotyrosine (NO2Tyr) and dityrosine (diTyr), specific molecular fingerprints of distinct oxidation pathways that convert LDL into an atherogenic form, are markedly enriched in human atheroma. Statins inhibit isoprenylation of key NAD (P) H oxidase components, leading to suppression in superoxide formation in vitro. The effects of statins on specific oxidation pathways in vivo are not known.
Methods: Subjects (n=35) with hypercholesterolemia and no known coronary artery disease were evaluated at baseline and following 12 weeks of therapy (atorvastatin, 10 mg/d). Plasma levels of protein-bound NO2Tyr and diTyr were determined by mass spectrometry, and compared with alterations in levels of LDL-cholesterol (LDL-C) and high sensitive C-reactive protein (hsCRP).
Results: Statin therapy caused significant reductions in the content (per mg plasma protein) of mean NO2Tyr and diTyr levels that were similar in magnitude to the reductions in mean LDL particle number (apoB-100) and total cholesterol (29% and 25%, respectively; P<0.001 each). No significant correlations were noted between statin-induced changes in diTyr or NO2Tyr and LDL-C or CRP.
Conclusion: Statins promote potent systemic anti-inflammatory and antioxidant effects independent of their influence on LDL and CRP.

Characteristics	Baseline (n = 35)	12 weeks (n = 35)	Absolute and Percentage change	P-Value
Dityrosine/tyrosine (micromole/mole)	34 ± 11	23 ± 7	-11 (32)	<0.001
Nitrotyrosine/tyrosine (micromole/mole)	15 ± 7	11 ± 5	-4 (25)	0.017
High sensitive C-reactive protein (mg/dL)	0.26 ± 0.32	0.23 ± 0.33	-0.2 (11)	0.096

1181-121 Does Secondary Prevention With Statins Eliminate the Risk of Hyperhomocysteinemia?

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Background: Hyperhomocysteinemia has emerged as a graded, independent risk factor for atherosclerosis. The molecular mechanism of vascular injury is uncertain. In a recent report, HMG CoA reductase mRNA and protein were found to be unregulated in human umbilical vein endothelial cells in response to increasing homocysteine (HCY) concentrations. Further, high HCY was associated with increased total cellular cholesterol content, and simvastatin reduced cellular cholesterol and prevented HCY-induced suppression of nitric oxide production.
Methods: We tested whether the mortality benefits of HMG CoA reductase inhibitors (statins) would be proportionately greater among coronary artery disease (CAD) patients with hyperhomocysteinemia. A total of 2,470 consecutive consenting patients who underwent angiography, had documented CAD, had a fasting HCY measurement, and were prospectively entered into the Intermountain Heart Collaborative Study Registry were studied. Multivariable Cox regressions were performed to assess the predictive value of HCY, statin use, and 15 other variables for survival.
Results: Average age was 65±11 years; 77% were men; 27% were discharged on a statin. During 3.8±1.6 years of follow-up, 379 (9.6%) died. HCY was higher among dying (median, 14.6 µmol/L) than surviving patients (13.0 µmol/L, p<0.001). The adjusted hazard ratio (HR) of death for HCY tertile 3 (>15.4 µmol/L) vs. 1 (<11.4 µmol/L) was 1.44 (CI=1.11-1.86,p=0.006). As expected, statin therapy reduced the risk of dying (HR=0.74, CI=0.45-0.96, p=0.02). However, proportionate reductions in mortality were no greater in the highest (HR=0.78) or middle (HR=0.74) than the lowest HCY tertile group (HR=0.68) (p>0.7 for statin*HCY interactions).
Conclusion: High HCY is confirmed to be an independent risk factor for patients with established CAD. However, HCY levels do not define patient groups with differential survival responses to statin therapy. Statins are indicated equally across the range of HCY plasma concentrations for secondary coronary prevention. Additional specific measures may be indicated for hyperhomocysteinemia.

1181-122 Statins Reduce the Incidence of Atrial Fibrillation in Patients With Coronary Artery Disease

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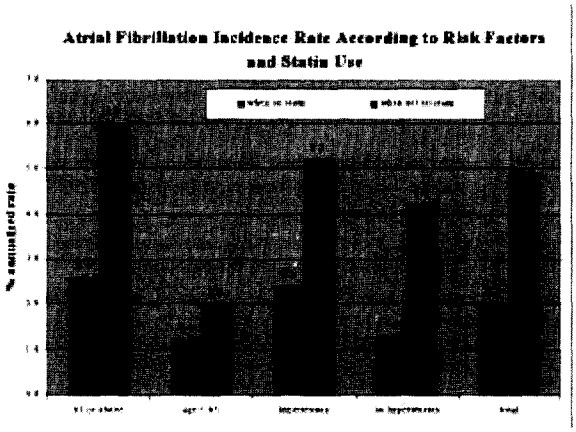
Background: Atrial Fibrillation (AF) is frequently associated factors that also predispose patients to the development of coronary artery disease (CAD). We hypothesized that statin therapy might have a beneficial effect on AF prevention in patients with CAD. **Methods**: The study cohort included patients with chronic stable CAD followed prospectively with annual questionnaires. Clinically documented AF episodes were recorded throughout the study. The exposure of interest was statins use. We calculated percent-annualized incidence rate and estimated the odds ratios (ORs) as well as 95% confidence intervals (CI). **Findings**: 482 study subjects had mean follow-up of four years and a maximum of seven years. A total of 130 episodes of AF occurred in 80 patients. Comparing the 132 patients who had continuous use of statins and 192 patients who did not use any cholesterol-lowering drugs, statin use was associated with lower percent-annualized incidence rate of AF (2 vs. 3.9). Comparison of the incidence rate on statin to the incidence rate when patients were not using statin revealed that statin use was associated with lower risk of having AF (OR, 0.41; 95% CI, 0.22-0.78). This association has remained significant after adjustment for potential confounders such as age, hypertension, diabetes, drug usage, and medical treatments.
Interpretations: Use of statins in patients with CAD appeared protective against AF by an unknown mechanism independent of cholesterol level and new cardiac events.



1181-123 Additive Effects of Ramipril and Atorvastatin on Inflammatory Cytokines Interferon-γ, Tumor Necrosis Factor-a, Interleukin-6, and C-Reactive Protein in Diabetic Patients With Congestive Heart Failure

Linda G. Tan, Stanley A. Tan, Lee S. Berk, Linda F. Lukman, Oakcrest Health Research Institute, Yucaipa, CA

Background: Interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α) and C-reactive protein (CRP) aggravate atherosclerosis and myocardial remodeling in CHF. Interleukin-6 (IL-6) increases CRP. Diabetic patients have increased IFN-γ, TNF-α, IL-6 and CRP, and higher incidence of CHF. Statins have been reported to decrease CRP, and ACE inhibitors regress myocardial hypertrophy in CHF.
Objective: We compared the effects of atorvastatin (A), ramipril (R), and combination of A+R on IFN-γ, TNF-α, IL-6 and CRP in diabetic patients with CHF.
Methods: 24 diabetics (hgb A_{1C} 7.1+1.3%) with CHF (EF<30%) were divided into two groups. Group A received A 40 mg/d, and group R 10 mg/d R. At 6 mo, R was added to group A, and A to group R. Lipid profile and the cytokines were measured and echocardiograms were performed at baseline and every 2 mo.
Results: Basal cytokines levels were above normal in all subjects. In group A, the LDL cholesterol decreased significantly at 2 mo. HDL rise and LVH regression were observed at 4 mo. IFN-γ, TNF-α & IL-6 decreased at 4 mo, and CRP at 6 mo. In group R, LVH regressed and EF improved significantly at 4 mo. IFN-γ, TNF-α and IL-6 decreased at 2 mo, and CRP at 4 mo. The magnitude of cytokines decreases were comparable in both group A & R. When R was added to group A, and A to group R, additive cytokine drops occurred. No significant changes in HDL, LDL, and total cholesterol were seen in group R. A lowered LDL cholesterol and increased HDL when added to group R, but no further improvement in CHF was noted. R significantly improved CHF and regressed LVH when added to group A.
Conclusions: Both A and R lower IFN-γ, TNF-α, IL-6 and CRP, and their effects are additive when combined. A lowers LDL and increases HDL, but only minimally improves CHF. R is a more potent LVH reducer and EF enhancer, but does not effect lipids. A+R are additive in lowering cytokines, potent lipid lowering agent, LVH reducer and EF enhancer. Thus combined atorvastatin and ramipril therapy can be beneficial for diabetic patients with CHF.